We claim:

1. A composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, which comprises a compound of the formula (I)

A-L-B (I)

in which

A is a monomer, multimer or polymer of TKPPR, or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate.

2. A composition according to claim 1, wherein A is a multimer of TKPPR or a TKPPR analogue.

3. A composition according to claim 2, wherein A is a tetramer of TKPPR or a TKPPR analogue.

4. A composition according to claim 1, wherein B comprises

B_1, a lipid able to bind the linker in a covalent or non-covalent manner.

5. A composition according to claim 4, in which B_1 comprises a synthetic or naturally-occurring generally amphipathic and biocompatible compound, selected from the group consisting of fatty acids; lysolipids; phospholipids; phosphatidylinositol; sphingolipids; glycolipids; glucolipids; sulfatides; glycosphingolipids; phosphatidic acids; lipids bearing polymers; lipids bearing sulfonated mono- di-, oligo- or polysaccharides; cholesterol, cholesterol sulfate; cholesterol hemisuccinate; tocopherol hemisuccinate; lipids with ether and ester-linked fatty acids; polymerized lipids; diacetyl phosphate; dicetyl phosphate; stearylamine; cardiolipin; phospholipids with short chain fatty acids of about 6 to about 8 carbons in length; synthetic phospholipids with asymmetric acyl chains; ceramides; non-ionic liposomes; sterol esters of sugar acids; esters of sugars and aliphatic acids; saponins; glycerol dilaurate; glycerol trilaurate; glycerol dipalmitate; glycerol; glycerol esters; long chain alcohols; 6-(5-cholesten-3β-yloxy)-1-thio-β-D-galactopyranoside; digalactosyl-diglyceride; 6-(5-cholesten-3 β-yloxy)hexyl-6-amino-6-deoxy-1-thio-β-D-galacto-pyranoside; 6-(5-cholesten-3 β-yloxy)hexyl-6-amino-6-deoxyl-1-thio- βD-manno-

pyranoside; 12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)octadecanoic acid; N-[12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)octadecanoyl]-2-aminopalmitic acid; N-succinyldioleylphosphatidylethanolamine; 1,2-dioleyl-sn-glycerol; 1,2-dipalmitoyl-sn-3-succinylglycerol; 1,3-dipalmitoyl-2-succinylglycerol; 1-hexadecyl-2-palmitoylglycerophosphoethanolamine; palmitoylhomocysteine, and combinations thereof.

6. A composition according to claim 1, wherein B comprises
B_2, a non-lipid polymer able to bind the linker in a covalent manner.

7. A composition according to claim 6, in which B_2 comprises B_{2a} a polymer useful for producing microparticles, or B_{2b}, a non-ionic surfactant.

8. A composition according to claim 7 in which B_{2a} is selected from the group consisting of polyvinyl alcohol (PVA) and a polyoxyethylene-polyoxypropylene block copolymer.

9. A composition according to claim 7, in which B_{2a} comprises a bead which is derivatizable and is attached to a detectable label.

10. A composition according to claim 9, in which the detectable label is a fluorescent or radioactive marker.

11. A composition according to claim 1, in which B comprises a bioactive agent.

12. A composition according to claim 1, in which B comprises a delivery vehicle for genetic material.

13. A composition according to claim 1, in which B comprises a delivery vehicle for a drug or therapeutic.

14. A composition according to claim 1, in which B comprises Bc, a metal chelating group.

15. A composition according to claim 14, in which the metal chelating group is complexed with a metal.

16. A composition according to claim ~~15~~, in which the metal chelating group is complexed with a radioactive metal.

17. A composition according to claim 16, in which the metal chelating group is complexed with a radioactive metal useful for radiotherapy.

18. A composition according to claim 16, in which the metal chelating group is complexed with a radioactive metal useful for imaging.

19. A composition according to claim 16, in which the metal is selected from the group consisting of: ^{99m}Tc, ^{67}Ga, ^{68}Ga, ^{111}In, ^{88}Y, ^{90}Y, ^{105}Rh, ^{153}Sm, ^{166}Ho, ^{165}Dy, ^{177}Lu, ^{64}Cu, ^{97}Ru, ^{103}Ru, ^{186}Re, and ^{188}Re.

20. A composition according to claim 14, in which the metal chelating group Bc is selected from the list consisting of: N_4, S_4, N_3S, N_2S_2 and NS_3 chelators.

21. A composition according to claim 20, in which the metal chelating group Bc comprises oxa-PnAO.

22. A composition according to claim 21, in which A comprises a tetramer of TKPPR and the metal chelating group is complexed to ^{99m}Tc.

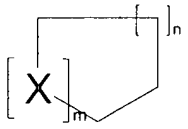
23. A composition according to claim 1, in which L is a bond or is derived from :

an alkyl chain C_1-C_{6000}, linear or branched, saturated or unsaturated, optionally interrupted or substituted by one or more groups such as: O, S, NR, OR, SR, COR, COOH, COOR, CONHR, CSNHR, C=O, S=O, $S(=O)_2$, $P=O(O)_2OR$, $P(O)_2(OR)_2$, halogens, or phenyl groups, optionally substituted by one or more -NHR, -OR, -SR, -COR, -CONHR, -N-C=S, -N-C=O, halogens, in which

R is H or an alkyl group C_1-C_4, linear or branched, optionally substituted by one or more –OH;

such a chain can be interrupted or substituted by one or more cyclic groups C_3-C_9, saturated or unsaturated, optionally interrupted by one or more O, S or NR; by one or more groups such as: -NHR, -OR, -SR, -COR, -CONHR, or a phenyl group optionally substituted by one or more -NHR, -OR, -SR, -COR, -CONHR, -N-C=S, -N-C=O, halogens.

24. A composition according to claim 23, in which the cyclic groups present in L are saturated or unsaturated, and correspond to the following general formula (III)



(III)

in which

n can range from 0 to 4;

m can range from 0 to 2;

X can be NH, NR, O, S or SR.

25. A composition according to claim 23, in which the linker L is an oligopeptide comprising 1 to 100 natural or synthetic amino acids.

26. A composition according to claim 25, in which the amino acids are selected from the group consisting of glycine, glutamic acid, aspartic acid, γ-amino-butyric acid and trans-4-aminomethyl-cyclohexane carboxylic acid.

27. A composition according to claim 23, in which L is derived from difunctional PEG-(polyethyleneglycol) derivatives.

28. A composition according to claim 23, in which L is selected from the group consisting of: glutaric acid, succinic acid, malonic acid, oxalic acid and PEG derivatized with two CH_2CO groups.

29. A compound of the formula (IIa) for use in targeting endothelial cells, tumor cells or other cells which express NP-1

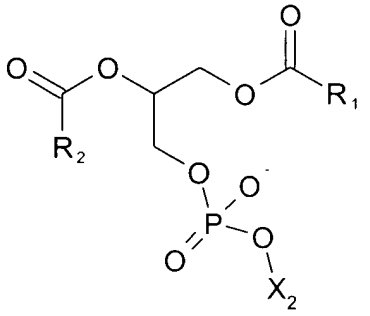
$$A\text{-}L\text{-}B_{1a} \quad \text{(IIa)}$$

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B_{1a} comprises a phospholipid moiety of the formula (II),



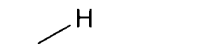
M (II)

where

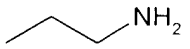
M is an alkaline or alkaline- earth metal cation;

R_1 and R_2 independently, correspond to a linear long chain C_{12}-C_{20}; saturated or unsaturated, optionally interrupted by C=O, or O; and

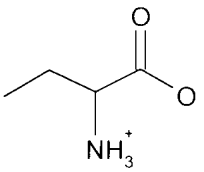
X_2 is selected in a group consisting of



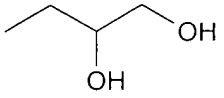
phosphatidic acid



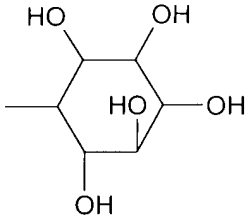
ethanolamine



serine



glycerol



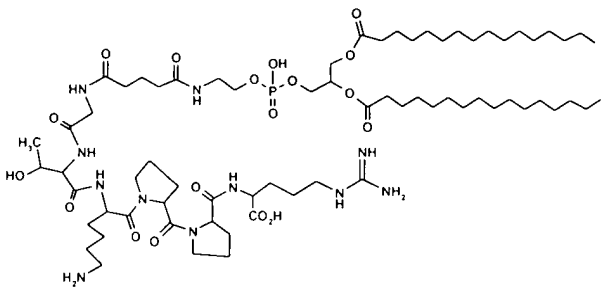
inositol

30. A compound according to claim 29, in which R_1 and R_2 are independently a saturated linear long chain C_{12}-C_{20}.

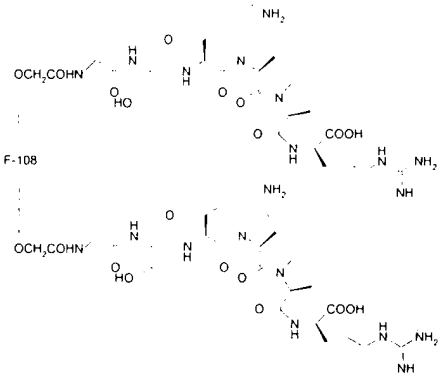
31. A compound according to claim 30, in which the phospholipid of formula (II) comprises a phospholipid selected from the group consisting of: dimyristoylphosphatidylethanolamine, dipalmitoylphosphatidylethanolamine, distearoylphosphatidylethanolamine, diarachidoylphosphatidylethanolamine, dioleylphosphatidylethanolamine, dilinoleylphosphatidylethanolamine, fluorinated analogues of any of the foregoing, and mixtures of any of the foregoing.

32. A compound according to claim 31, in which the phospholipid of formula (II) comprises dipalmitoylphosphatidylethanolamine.

33. A composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, comprising a compound selected from the group consisting of:



and



34. An ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of any one of claims 29 to 32.

35. An ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of claim 29 and the gas comprises a fluorinated gas.

36. An ultrasound contrast agent comprising a suspension of gas-filled microbubbles in which the microbubbles comprise a compound of claim 29 in which A is TKPPR tetramer and the gas comprises SF_6 or a perfluorocarbon selected from the group consisting of C_3F_8, C_4F_8, C_4F_{10}, C_5F_{12}, C_6F_{12}, C_7F_{14} and C_8F_{18}.

37. A compound for use in targeting endothelial cells, tumor cells or other cells that express NP-1 of the formula

$$A\text{-}L\text{-}B_3$$

where

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B_3 is a biodegradable, physiologically acceptable polymer.

38. An ultrasound contrast agent comprising a suspension of gas-filled microballoons, in which the microballoons comprise a compound of claim 37.

39. An ultrasound contrast agent comprising a suspension of gas-filled microballoons, in which the microballoons comprise a compound of claim 37 in which A is a TKPPR tetramer and the gas comprises a gas selected from the group consisting of: air; nitrogen; oxygen; CO_2; argon; xenon or krypton,a fluorinated gas, a low molecular weight hydrocarbon, an alkene or an alkyne and mixtures thereof.

40. A compound for use for use in targeting endothelial cells, tumor cells or other cells which express NP-1 comprising a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1or cells that express NP-1 with avidity that is equal to or greater than TKPPR.

41. A compound for use in inhibiting angiogenesis comprising a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR.

42. A pharmaceutical composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, comprising:

a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR; and

a pharmaceutically acceptable carrier.

43. A pharmaceutical composition for use in inhibiting angiogenesis comprising:

a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR; and

a pharmaceutically acceptable carrier.

44. A pharmaceutical composition for use in inhibiting angiogenesis comprising:

a tetramer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR; and

a pharmaceutically acceptable carrier.

45. A process for preparing a compound of claim 1 comprising:

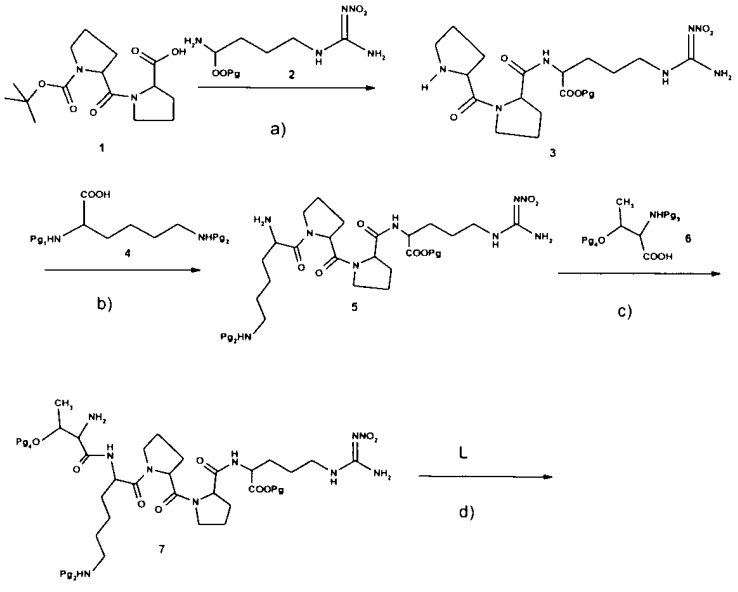
a) obtaining a monomer, multimer or polymer of TKPPR or an analogue thereof;

b) conjugating the monomer, multimer or polymer of TKPPR with the linker to give a compound of formula (IIb) ; and

A-L (IIb)

c) forming a covalent or non-covalent bond between a compound of formula (IIb) and the substrate B or forming a covalent bond between the substrate B and the linker to form a conjugate B-L, and
conjugating of the conjugate B-L with the monomer, multimer or polymer of TKPPR or an analogue thereof.

46. A process according to claim 45, in which the compounds of formula (IIb) are prepared as illustrated in the following Scheme



in which

the steps a), b), and c) are all condensation reactions performed under basic conditions, and step d) is a condensation in basic conditions with the linker.

47. A method of imaging an angiogenic site in an human or animal comprising:

a) administering to said human or animal a composition comprising a compound of the formula (I)

A-L-B (I)

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate, where B comprises a detectable moiety; and

b) detecting said moiety.

48. A method of imaging endothelial cells, tumor cells or other cells that express NP-1 in a human or animal comprising:

a) administering to said human or animal a composition comprising a compound of the formula (I)

A-L-B (I)

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate, where B comprises a detectable moiety; and

b) detecting said moiety.

49. A method of ultrasound imaging comprising administering an ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of the formula (IIa)

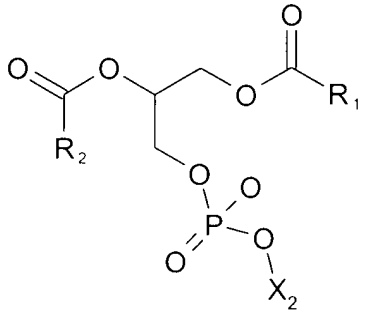
$A\text{-}L\text{-}B_{1a}$ (IIa)

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B_{1a} comprises a phospholipid moiety of the formula (II),



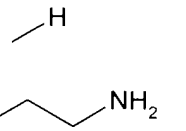
M (II)

where

M is an alkaline or alkaline- earth metal cation;

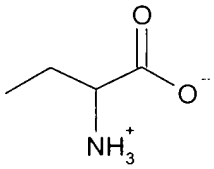
R_1 and R_2 independently, correspond to a linear long chain C_{12}-C_{20}; saturated or unsaturated, optionally interrupted by C=O, or O; and

X_2 is selected in a group consisting of

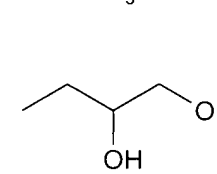


phosphatidic acid

ethanolamine

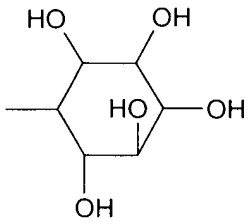


serine



glycerol

inositol



50. A method of staging a tumor in a human or an animal comprising administering a composition comprising a detectable moiety and a compound of claim 1 to said human or animal and detecting said moiety in said human or animal.

51. A method of screening at least one agent for the ability of said agent to target endothelial cells, tumor cells or other cells that express NP-1, comprising contacting said cells in vitro with a composition of any one of claims 7 to 9.

52. A method of screening at least one targeted ultrasound contrast agent for the ability of said agent to target endothelial cells, tumor cells or other cells that express NP-1, comprising contacting said cells in vitro with a composition of any one of claims 7 to 9.

53. A method for the therapeutic delivery in vivo of a bioactive agent to a patient suffering from effects associated with angiogenesis-related disorders comprising administering a therapeutically effective amount of a composition of any one of claims 11 to 13.

54. A method of treating an individual exhibiting effects of an angiogenesis-related disorder comprising administering a therapeutically effective amount of a composition of any one of claims 11 to 13.

55. A composition according to claim 12, wherein B comprises a delivery vehicle for genetic material selected from the group consisting of: a virus particle, a viral or retroviral gene therapy vector, a liposome, a complex of cationic lipids and genetic material and a complex of dextran derivatives and genetic material.

56. A method for delivering desired nucleic acids to endothelial cells, tumor cells or other cells expressing NP-1, comprising administering a therapeutically effective amount of the composition of claim 55.

57. A method of enhancing endothelial cell-targeted gene therapy comprising incorporating compounds of claim 40 in or on the delivery vehicle for genetic material.

58. A method of enhancing tumor cell-targeted gene therapy comprising incorporating compounds of claim 40 in or on the delivery vehicle for genetic material.

59. A method of enhancing gene therapy targeting angiogenic cells comprising incorporating compounds of claim 41 in or on the delivery vehicle for genetic material.

60. A method for imaging of a human or animal comprising:

a) administering to said human or animal a composition according to any one of claims 16,18,19,21 or 22; and

b) imaging all or part of said human or animal using a camera that detects radiation.

61. A method for imaging of a human or animal comprising:

a) administering to said human or animal a composition according to claim 21; and

b) imaging all or part of said human or animal using a camera that detects radiation.

62. A method for treating a human or animal with a tumor or angiogenesis-related disease comprising administering to said human or animal a therapeutically effective amount of a composition according to either one of claims 17 or 19.

63. A kit for preparing a radiopharmaceutical comprising a composition of claim 14 or a pharmaceutically acceptable salt thereof.

64. A kit according to claim 63, further comprising an exchange ligand.

65. A kit according to either claim 63 or 64, further comprising a reducing agent.